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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| RAE, CHARLESWORTH E | |
| ART UNIT | PAPER NUMBER |
| 1614 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/595,709 | GRASES FREIXEDAS, FELICIA | |
| | Examiner | Art Unit | |
| | Charlesworth Rae | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2006* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### Status of the Claims

Claims 1-7 are currently pending in this application and are the subject of the Office action.

### Priority

Receipt is acknowledged of papers submitted under 35 USC 119(a)-(d), which are made of record. It is noted that the certified foreign priority document filed 5/05/06 is in a foreign language other than English. In the absence of the English translation, the effective filing date of the instant application is considered to be the filing date of the international application: 11/3/04.

### Rejection under 101

35 USC 101 reads as follows

> Whoever invents or discovers any new and useful process, machine, manufacturer, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 USC 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process claim under 35 USC 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner,* 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 provide for the use of a composition including myo-inostiol hexaphosphate in a form adapted to topical administration for the manufacture of a formulation for the prevention and/or treatment of a disease associated with the development of heterogenous nucleants which induce the development of pathological calcification in a soft tissue.

Claim 1 recites the term "and/or." This term is indefinite as the term could reasonably construed to have two mutually exclusive different meanings.

**Claim rejections – 35 USC 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 USC 102(b) as being anticipated by Znaiden et al. (US Patent Application 5,268,176).

For purposes of this rejection, the instant claims are being construed as method of prevention or treatment claims.

Znaiden et al. teach topical compositions containing inositol hexaphopshate (phytic acid or myo-inositol) for use in the treatment of telangiectasia (or spider veins),

which is characterized by the visual dilation of one or more superficial skin arterioles in the human body (col. 1, line 16 to col. col. 4, line 46). Claim 1 recites a composition including the identical active compound as taught by Znaiden i.e. myo-inositol, for use in the prevention and/or treatment of a disease associated with the development of heterogenous nucleants which induce the development of pathological calcification in a soft tissue. To the extent that claim 1 recites the identical active compound for topical administration to a soft tissue (e.g. spider veins), the contemplated treatment effect of the instant invention is deemed to be an inherent characteristic of topically administering the identical composition. Similarly, the limitations recited in claims 2-7 (e.g. *"wherein the disease is associated with the development of calcifications in a soft tissue;" "which said disease consists on an arterial calcifcation;" "which said disease consists on a renal calcification;" "which said disease consists on a cerebral calcification;" "in which said disease consists pm a pulmonary calcification"*) are also considered to be inherent features.

**Relevant Art of Record**

The below cited art made of record and relied upon is considered pertinent to applicant's invention.

Galvin et al. (US Patent 6,359,194) teach methods for screening compounds and other substances for treating cardiovascular disease symptoms, including cardiac calcification, hemorrhagic telangiectasia, advanced atherosclerosis and/or plaque rupture, cardiovascular calcification (col. 8, line 64 to col. 9, line 22).

**Claim Rejections – 35 USC 112 – First Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for methods of preparing and methods of use of myo-inositol compositions for treating certain diseases associated with the development of heterogenous nucleants which induce the development of pathological calcification in a soft tissue, does not reasonably provide enablement for preventing said diseases and/or treating any and all diseases associated with the development of heterogenous nucleants which induce the development of pathological calcification in a soft tissue. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art.

The invention in general relates to a the use of myo-inositol compositions for topical administration for treating diseases associated with the development of

heterogenous nucleants which induce the development of pathological calcification in a soft tissue.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. It is noted that the chemical and medical arts are generally unpredictable, requiring each embodiment to be individually assessed for chemical, pharmacologic, pharmaceutical, and clinical efficacy. The more unpredictable an area, the more specific enablement is necessary in order to satisfy the statue. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)).

Grases et al. teach that pathological calcification in soft tissues (i.e.ectopic clacification) can have severe consequences when it occurs in vital organs such as the vascular or renal systems (Grases et al. Effect of crystallization inhibitors on vascular clacifcaqtions induced by vitamin D : A Pilot study in Sprague-Dawley rats. Cir. J. 2007;71:1152-1156; see especially page 1152, col. 1, first para.). Grases et al. teach that in general, the development of tissue clacification requires a preexisting injury as an inducer (**heterogenous nucleant**), whereas further progression requires the presence of other promoter factors (such as hypercalcemia and/or hyperphosphatemia) and/or a deficiency in calcification repressors factors (crystallization inhibitors and cellular defense mechanisms); see page 1152, col. 1, second para.). Grases et al. teach that pyrophosphate, biphosphonates and phytate (myo-inositol hexakisphosphate) have been shown to inhibit crystallization in the form of vascular calcification (page 1152, col. 2, last para.). Grases et al. also teach that based on the fact that phytate was found to

act as vascular calcification inhibitor, the action of polyphosphates could be important in protecting against vascular calcification (page 155, last para.).

2. The breadth of the claims

The instant claims are relatively broad in scope. For example, claim 1 recites the language "disease associate with the development of heterogenous nucleants." However, the disclosure does not to provide any definition of the term "heterogenous nucleants," or discloses the connection between the administration of myo-inositol hexaphosphate and its effect on heterogenous nucleants, or how the effect on heterogenous nucleants relates to the contemplated effects to be achieved in practicing the instant invention. Claim 1 also recites the term "pathological calcification in a soft tissue," which encompasses pathological calcification in soft tissues of any and all mammalian species. Because the therapeutic response to be achieved would reasonably vary depending upon the specific mammalian specie, targeted soft tissue, location of the soft tissue, and the pharmacodynamic/pharmacokinetic profile of myo-inositol hexaphosphate, the level of predictably in practicing the claimed invention would be greatly diminished.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification discloses study results involving the topical administration of phytate to rats (pages 6-10). Based on the instant disclosure, the applicant at best has provided specific direction or guidance only for a general method of using a myo-inositol composition. Further, extrapolation of the exemplified rat data

disclosed by applicant to any and all mammalian species would reasonably require extensive experimentation in order to achieve the contemplated treatment effects in practicing the instant claimed invention commensurate the claims.

4. The quantity of experimentation necessary

In view of the uncertainty and unpredictability of the art as evidenced by the discussion of the prior art, it is reasonable to surmise that this level of uncertainty in the art would require one skilled in the art to conduct more than routine experimentation in order to practice the claimed invention commensurate with the scope of the claims.

For the reasons stated above, claims 1-7 are rejected under 35 USC 112, first paragraph, for lack of scope enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

27 September 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER